10/630,344

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	964	(435/7.24).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:51
L2	248	(435/40.51).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:52
L3	1921	(436/63).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:53
L4	2224	(435/29).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/04/24 16:53
L5	4824	L1 OR L2 OR L3 OR L4	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L6	2000	ANGINA?	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L7	342	STENOCARDIA	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L8	6	CORONARISM	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:54
L9	7	CARDIAGRA	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L10	2345	L6 OR L7 OR L8 OR L9	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L11	51078	INTERLEUKIN	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55

EAST Search History

L12	47077	INTERFERON	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L13	63027	CYTOKINE	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:55
L14	13903	LYMPHOKINE	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:56
L15	98453	L11 OR L12 OR L13 OR L14	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:56
L16	3	L5 AND L10 AND L15	US-PGPUB; USPAT; EPO; DERWENT	ADJ	ON	2006/04/24 16:56

10/630,344

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 12:06:48 ON 24 APR 2006

=> FILE MEDLINE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 12:07:02 ON 24 APR 2006

FILE LAST UPDATED: 22 APR 2006 (20060422/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> S ANGINA?
L1        48229 ANGINA?

=> S STENOCARDIA
            828 STENOCARDIA
             20 STENOCARDIAS
L2           847 STENOCARDIA
                 (STENOCARDIA OR STENOCARDIAS)

=> S CORONARISM
              0 CORONARISM
L3            0 CORONARISM

=> S CARDIAGRA
              0 CARDIAGRA
L4            0 CARDIAGRA

=> S L1 OR L2
L5        48317 L1 OR L2

=> S INTERLEUKIN
         144796 INTERLEUKIN
           7421 INTERLEUKINS
L6       147358 INTERLEUKIN
                 (INTERLEUKIN OR INTERLEUKINS)

=> S INTERFERON
          92119 INTERFERON
          19791 INTERFERONS
L7        97261 INTERFERON
```

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                (INTERFERON OR INTERFERONS)

=> S CYTOKINE
         75299 CYTOKINE
         96297 CYTOKINES
L8      132678 CYTOKINE
                (CYTOKINE OR CYTOKINES)

=> S LYMPHOKINE
          9068 LYMPHOKINE
         18810 LYMPHOKINES
L9       25166 LYMPHOKINE
                (LYMPHOKINE OR LYMPHOKINES)

=> S L6 OR L7 OR L8 OR L9
L10     288379 L6 OR L7 OR L8 OR L9

=> T(W)(CELL OR LYMPHOCYTE)
T(W)(CELL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> S  T(W)(CELL OR LYMPHOCYTE)
        4176845 T
        2000119 CELL
        1807454 CELLS
        2663835 CELL
                (CELL OR CELLS)
         195552 LYMPHOCYTE
         331266 LYMPHOCYTES
         390516 LYMPHOCYTE
                (LYMPHOCYTE OR LYMPHOCYTES)
L11      257834 T(W)(CELL OR LYMPHOCYTE)

=> S L5 AND L10 AND L11
L12          57 L5 AND L10 AND L11

=> S L12 NOT 2001-2006/PY
       3043636 2001-2006/PY
                (20010000-20069999/PY)
L13          13 L12 NOT 2001-2006/PY

=> SAVE TEMP
ENTER L#, L# RANGE, ALL, OR (END):L13
ENTER NAME OR (END):ANGINA/A
ANSWER SET L13 HAS BEEN SAVED AS 'ANGINA/A'

=> D L13 1-13 BIB AB

L13  ANSWER 1 OF 13     MEDLINE on STN
AN   2000329934     MEDLINE
DN   PubMed ID: 10869258
TI   Monoclonal T-cell proliferation and plaque instability
     in acute coronary syndromes.
AU   Liuzzo G; Goronzy J J; Yang H; Kopecky S L; Holmes D R; Frye R L; Weyand C
     M
CS   Department of Medicine, Division of Rheumatology, Mayo Clinic and
     Foundation, Rochester, MN 55905, USA.
NC   RO1-AR41974 (NIAMS)
     RO1-AR42527 (NIAMS)
     RO1EY11916 (NEI)
SO   Circulation, (2000 Jun 27) Vol. 101, No. 25, pp. 2883-8.
     Journal code: 0147763. E-ISSN: 1524-4539.
CY   United States
```

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200007
ED Entered STN: 28 Jul 2000
Last Updated on STN: 21 May 2001
Entered Medline: 19 Jul 2000
AB BACKGROUND: Unstable **angina** (UA) is associated with systemic inflammation and with expansion of **interferon**-gamma-producing **T lymphocytes**. The cause of **T-cell** activation and the precise role of activated **T cells** in plaque instability are not understood. METHODS AND RESULTS: Peripheral blood **T cells** from 34 patients with stable **angina** and 34 patients with UA were compared for the distribution of functional **T-cell** subsets by flow cytometric analysis. Clonality within the **T-cell** compartment was identified by **T-cell** receptor spectrotyping and subsequent sequencing. Tissue-infiltrating **T cells** were examined in extracts from coronary arteries containing stable or unstable plaque. The subset of CD4(+)CD28(null) **T cells** was expanded in patients with UA and infrequent in patients with stable **angina** (median frequencies: 10.8% versus 1.5%, P<0.001). CD4(+)CD28(null) **T cells** included a large monoclonal population, with 59 clonotypes isolated from 20 UA patients. **T-cell** clonotypes from different UA patients used antigen receptors with similar sequences. **T-cell** receptor sequences derived from monoclonal **T-cell** populations were detected in the culprit but not in the nonculprit lesion of a patient with fatal myocardial infarction. CONCLUSIONS: UA is associated with the emergence of monoclonal **T-cell** populations, analogous to monoclonal gammopathy of unknown significance. Shared **T-cell** receptor sequences in clonotypes of different patients implicate chronic stimulation by a common antigen, for example, persistent infection. The unstable plaque but not the stable plaque is invaded by clonally expanded **T cells**, suggesting a direct involvement of these lymphocytes in plaque disruption.

L13 ANSWER 2 OF 13 MEDLINE on STN
AN 2000288058 MEDLINE
DN PubMed ID: 10829249
TI Inflammation and acute coronary syndromes.
AU Biasucci L M; Liuzzo G; Angiolillo D J; Sperti G; Maseri A
CS Institute of Cardiology, Catholic University, Rome, Italy.. biasucci@pelagus.it
SO Herz, (2000 Mar) Vol. 25, No. 2, pp. 108-12. Ref: 46
Journal code: 7801231. ISSN: 0340-9937.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200006
ED Entered STN: 6 Jul 2000
Last Updated on STN: 6 Jul 2000
Entered Medline: 23 Jun 2000
AB The presence of inflammatory infiltrates in unstable coronary plaques suggests that inflammatory processes may contribute to the pathogenesis of these syndromes. In patients with unstable **angina**, coronary atherosclerotic plaques are characterized by the presence of macrophages, and to a lesser extent, **T-lymphocytes**, at the immediate site of either plaque rupture or superficial erosion; moreover, the rupture-related inflammatory cells are activated, indicating ongoing inflammation at the site of plaque disruption. These observations are confirmed by clinical studies demonstrating activated circulating neutrophils, lymphocytes and monocytes, and increased concentrations of

pro-inflammatory **cytokines**, such as **interleukin** (IL) 1 and 6, and of acute phase reactants in patients with unstable **angina** and myocardial infarction. In particular elevated levels of C-reactive protein are associated with an increased risk of in-hospital and 1 to 2 years new coronary events in patients with unstable **angina**, but are also associated with an increased long-term risk of death and myocardial infarction in apparently normal subjects. Thus, accumulating evidence suggests that inflammation may cause local endothelial activation and, possibly, plaque fissure, leading to unstable **angina** and infarction. Although no information is yet available on the causes of inflammation and on its localization, these novel lines of research may open the way to a different approach to the patient with acute coronary syndromes.

L13 ANSWER 3 OF 13 MEDLINE on STN
AN 2000225898 MEDLINE
DN PubMed ID: 10762452
TI Changing concepts of atherogenesis.
AU Libby P
CS Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA.. plibby@rics.bwh.harvard.edu
NC HL34636 (NHLBI)
SO Journal of internal medicine, (2000 Mar) Vol. 247, No. 3, pp. 349-58.
Ref: 85
Journal code: 8904841. ISSN: 0954-6820.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 200005
ED Entered STN: 25 May 2000
Last Updated on STN: 25 May 2000
Entered Medline: 12 May 2000
AB This review discusses three stages in the life history of an atheroma: initiation, progression and complication. Recruitment of mononuclear leucocytes to the intima characterizes initiation of the atherosclerotic lesion. Specific adhesion molecules expressed on the surface of vascular endothelial cells mediate leucocyte adhesion: the selectins and members of the immunoglobulin superfamily such as vascular cell adhesion molecule-1 (VCAM-1). Once adherent, the leucocytes enter the artery wall directed by chemoattractant chemokines such as macrophage chemoattractant protein-1 (MCP-1). Modified lipoproteins contain oxidized phospholipids which can elicit expression of adhesion molecule and **cytokines** implicated in early atherogenesis. Progression of atheroma involves accumulation of smooth muscle cells which elaborate extracellular matrix macromolecules. These processes appear to result from an eventual net positive balance of growth stimulatory versus growth inhibitory stimuli, including proteins (**cytokines** and growth factors) and small molecules (e.g. prostanoids and nitric oxide). The clinically important complications of atheroma usually involve thrombosis. Arterial stenoses by themselves seldom cause acute unstable **angina** or acute myocardial infarction. Indeed, sizeable atheroma may remain silent for decades or produce only stable symptoms such as **angina** pectoris precipitated by increased demand. Recent research has furnished new insight into the molecular mechanisms that cause transition from the chronic to the acute phase of atherosclerosis. Thrombus formation usually occurs because of a physical disruption of atherosclerotic plaque. The majority of coronary thromboses result from a rupture of the plaque's protective fibrous cap, which permits contact between blood and the highly thrombogenic material located in the lesion's lipid core, e.g. tissue factor. Interstitial collagen accounts for most of the tensile strength of the plaque's fibrous cap. The amount of collagen in the lesion's fibrous cap depends upon its rate of biosynthesis stimulated by factors released from platelets (e.g. transforming growth factor beta or

platelet-derived growth factor), but inhibited by gamma **interferon**
, a product of activated **T cells** found in plaques.
Degradation by specialized enzymes (matrix metalloproteinases) also
influences the level of collagen in the plaque's fibrous cap. Such
studies illustrate how the application of cellular and molecular
approaches has fostered a deeper understanding of the pathogenesis of
atherosclerosis. This increased knowledge of the basic mechanisms enables
us to understand how current therapies for atherosclerosis may act.
Moreover, the insights derived from recent scientific advances should aid
the discovery of new therapeutic targets that would stimulate development
of novel treatments. Such new treatments could further reduce the
considerable burden of morbidity and mortality due to this modern scourge,
and reduce reliance on costly technologies that address the symptoms
rather than the cause of atherosclerosis.

L13 ANSWER 4 OF 13 MEDLINE on STN
AN 2000040177 MEDLINE
DN PubMed ID: 10571971
TI Perturbation of the **T-cell** repertoire in patients with
unstable **angina.**
AU Liuzzo G; Kopecky S L; Frye R L; O'Fallon W M; Maseri A; Goronzy J J;
Weyand C M
CS Department of Medicine, Mayo Clinic, Rochester, MN 55905, USA.
SO Circulation, (1999 Nov 23) Vol. 100, No. 21, pp. 2135-9.
Journal code: 0147763. E-ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199912
ED Entered STN: 13 Jan 2000
Last Updated on STN: 21 May 2001
Entered Medline: 9 Dec 1999
AB BACKGROUND: Monocytes are constitutively activated in unstable
angina (UA), resulting in the production of IL-6 and the
upregulation of acute phase proteins. Underlying mechanisms are not
understood. To explore whether the production of the potent monocyte
activator IFN-gamma is altered in UA, we compared **cytokine**
production by **T lymphocytes** in patients with UA
(Braunwald's class IIIB) and with stable **angina** (SA). METHODS
AND RESULTS: Peripheral blood lymphocytes were collected at the time of
hospitalization and after 2 and 12 weeks. **Cytokine**-producing
CD4(+) and CD8(+) **T cells** were quantified by 3-color
flow cytometry after stimulation with phorbol myristate acetate and
ionomycin. UA was associated with an increased number of CD4(+) and
CD8(+) **T cells** producing IFN-gamma, whereas patients
with SA had higher frequencies of IL-2(+) and IL-4(+) CD4(+) **T**
cells. Expansion of the IFN-gamma(+) **T-cell**
population in UA persisted for at least 3 months. Increased production of
IFN-gamma in UA could be attributed to the expansion of an unusual subset
of **T cells**, CD4(+)CD28(null) **T cells**
. CONCLUSIONS: Patients with UA are characterized by a perturbation of
the functional **T-cell** repertoire with a bias toward
IFN-gamma production, suggesting that monocyte activation and acute phase
responses are consequences of **T-cell** activation.
IFN-gamma is produced by CD4(+)CD28(null) **T cells**,
which are expanded in UA and distinctly low in SA and controls. The
emergence of CD4(+)CD28(null) **T cells** may result from
persistent antigenic stimulation.

L13 ANSWER 5 OF 13 MEDLINE on STN
AN 2000017427 MEDLINE
DN PubMed ID: 10551265
TI Activation of monocytes, **T-lymphocytes** and plasma
inflammatory markers in **angina** patients.

AU Lee W H; Lee Y; Kim J R; Chu J A; Lee S Y; Jung J O; Kim J S; Kim S; Seo J D; Rhee S S; Park J E
CS Clinical Research Center, Samsung Biomedical Research Institute, Seoul, Korea.
SO Experimental & molecular medicine, (1999 Sep 30) Vol. 31, No. 3, pp. 159-64.
Journal code: 9607880. ISSN: 1226-3613.
CY KOREA (SOUTH)
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199911
ED Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 23 Nov 1999
AB Inflammation and activation of immune cells have important roles in the pathogenesis of atherosclerosis. We analyzed the plasma levels of inflammatory markers and the degree of activation of peripheral blood monocytes and **T-lymphocytes** isolated from 12 unstable **angina**, 12 stable **angina**, and 12 normal subjects. In 20%-33% of patients, monocytes expressed high basal levels of IL-8, tissue factor, IL-1beta, and monocyte chemoattractant protein-1 mRNA. Furthermore, basal mRNA levels of these **cytokines** showed strong correlation with each other ($p < 0.01$ in all combination) but not with tumor necrosis factor-alpha or transforming growth factor-beta1. Plasma level of C-reactive protein was highest in the unstable **angina** patients (1.63+/-0.70 mg/l) and lowest in the control subjects (0.22+/-0.08 mg/l) ($P = 0.03$). We also observed a high correlation between C-reactive protein level and the occurrence of minor and major coronary events during 6 months of follow-up. Activation status of **T-cells**, assessed by the percentage of HLA-DR positive cells, was highest in the unstable **angina** patients (26.8+/-1.4%) compared with that in the control (14.7+/-1.2%) ($P = 0.0053$). Our data represent the first case showing that the circulating monocytes in **angina** patients are activated to a state express numerous proatherogenic **cytokines.** These results may help to diagnose **angina** patients according to the inflammatory markers and evaluate the prognosis of the disease.

L13 ANSWER 6 OF 13 MEDLINE on STN
AN 1999417068 MEDLINE
DN PubMed ID: 10488965
TI Plasma levels of **interleukin** 2, 6, 10 and phenotypic characterization of circulating **T lymphocytes** in ischemic heart disease.
AU Mazzone A; De Servi S; Vezzoli M; Fossati G; Mazzucchelli I; Gritti D; Ottini E; Mussini A; Specchia G
CS Department of Internal Medicine and Therapeutics, University of Pavia, IRCCS S. Matteo Hospital, Italy.. a.mazzone@smatteo.pv.it
SO Atherosclerosis, (1999 Aug) Vol. 145, No. 2, pp. 369-74.
Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 26 Oct 1999
Last Updated on STN: 26 Oct 1999
Entered Medline: 13 Oct 1999
AB The purpose of this study was to assess lymphocyte receptors expression in patients with ischemic heart diseases, as well as to measure the plasma levels of **interleukin** (IL) 2, 6 and 10. **T Lymphocytes** are found in large numbers in human atherosclerotic plaques, indicating that immune and inflammatory mechanisms are important factors in the pathogenesis of atherosclerosis. Recent data have also

implicated **T lymphocytes** in the pathogenetic mechanism of unstable **angina** and ischemic heart disease. Three groups of patients were studied: 42 with an acute ischemic syndrome (AIS), 36 with stable **angina** (SA) and 39 healthy controls. To characterize lymphocyte phenotype, flow cytometry was performed in whole-blood samples. IL-2, IL-6 and IL-10 were measured using the ELISA method. Double fluorescence evaluation showed an increase in CD8+/CD11b+ cells (cytotoxic **T lymphocytes**) and in CD11b+/CD16+CD56+ cells (NK lymphocytes) in the AIS group and in SA group as compared to the control group ($P < 0.05$ and $P < 0.001$, respectively). IL-2 was increased in the AIS and SA groups compared to the control group (AIS 4.5 +/- 0.5 pg/ml; SA 6.3 +/- 0.6 pg/ml; controls 2.4 +/- 0.8 pg/ml, $P < 0.05$), whereas IL-6 was higher in the AIS group than in the other two groups (AIS 10.8 +/- 1.8 pg/ml; SA 1.8 +/- 0.8 pg/ml; controls 1.2 +/- 0.6 pg/ml, $P < 0.0001$). These data show that patients with ischemic heart disease have an increase in circulating cytotoxic **T lymphocytes** and in IL-2 plasma levels, irrespective of their clinical presentation, compared to normal control subjects, whereas IL-6 is elevated only in patients with AIS.

L13 ANSWER 7 OF 13 MEDLINE on STN
AN 1999025811 MEDLINE
DN PubMed ID: 9809939
TI Immune system activation follows inflammation in unstable **angina** : pathogenetic implications.
AU Caligiuri G; Liuzzo G; Biasucci L M; Maseri A
CS Department of Cardiology, Catholic University, Rome, Italy.. giuseppina.caligiuri@cmm.ki.se
SO Journal of the American College of Cardiology, (1998 Nov) Vol. 32, No. 5, pp. 1295-304.
Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199811
ED Entered STN: 6 Jan 1999
Last Updated on STN: 6 Jan 1999
Entered Medline: 20 Nov 1998
AB OBJECTIVES: The aim of this study was to assess the relations between inflammation, specific immune response and clinical course in unstable **angina** (UA). BACKGROUND: Several studies suggest that either inflammation and/or **T-cell** activation might have a pathogenetic role in UA, but neither their potential reciprocal connection nor their relation to the clinical course is known. METHODS: Serum levels of C-reactive protein (CRP) (inflammation), IgG, IgA, IgM, C3, C4 (humoral immunity), IL-2 and the percentage of CD4+, CD8+ and CD3+/DR+ **T-cells** (cell-mediated immunity) were measured in 35 patients with UA and 35 patients with chronic stable **angina** (CSA) during a period of 6 months. RESULTS: The CRP levels and the main specific immune markers (CD4+ and CD3+/DR+ cells, IL-2 and IgM) were higher in unstable than in stable **angina**. In UA, the serum levels of IgM and IL-2 and the percentage of double positive CD3+/DR+ significantly increased at 7 to 15 days, and returned to baseline at 6 months. The increment of circulating activated **T cells** (CD3+/ DR+) in UA was inversely related to the admission levels of CRP ($r=-0.63$, $p=0.003$) and associated with a better outcome. CONCLUSIONS: Our data suggest that the inflammatory component systemically detectable in UA may be antigen-related and that the magnitude of the immune response correlates with the clinical outcome of instability.

L13 ANSWER 8 OF 13 MEDLINE on STN
AN 1998436543 MEDLINE
DN PubMed ID: 9764052
TI Recent activation of the plaque immune response in coronary lesions

underlying acute coronary syndromes.
AU van der Wal A C; Piek J J; de Boer O J; Koch K T; Teeling P; van der Loos C M; Becker A E
CS Department of Cardiovascular Pathology, University of Amsterdam, Netherlands.
SO Heart (British Cardiac Society), (1998 Jul) Vol. 80, No. 1, pp. 14-8. Journal code: 9602087. ISSN: 1355-6037.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199810
ED Entered STN: 21 Oct 1998
Last Updated on STN: 21 Oct 1998
Entered Medline: 14 Oct 1998
AB OBJECTIVE: To discriminate between chronic inflammation and acute activation of the plaque immune response in culprit lesions of patients with acute coronary syndromes. DESIGN: Retrospective study. SETTING: Tertiary referral centre. SUBJECTS: 71 patients having coronary atherectomy were classified according to their ischaemic syndrome: stable **angina** (n = 23); stabilised unstable **angina** (n = 18); refractory unstable **angina** (n = 11); and acute myocardial infarction (n = 19). MAIN OUTCOME MEASURES: Immunohistochemical measurement of **interleukin** 2 receptor (IL-2R) (CD25) positive cells expressed as a percentage of the total amount of (CD3 positive) **T lymphocytes** in frozen sections of atherectomy specimens. RESULTS: The number of lesions containing IL-2R (CD25) positive **T cells** increased with severity of the ischaemic coronary syndrome (stable **angina**, 52%; stabilised unstable **angina**, 77.8%; refractory unstable **angina**, 90.9%; acute myocardial infarction, 89.4%). The percentage of activated **T cells** (CD25/CD3 ratios x100) increased in lesions associated with refractory unstable **angina** (7.8%) and acute myocardial infarction (18.5%), compared with those in lesions associated with either chronic stable **angina** (2.2%) or stabilised unstable **angina** (3.3%). CONCLUSIONS: An increase in the percentage of IL-2R positive **T lymphocytes** in culprit lesions of patients with acute coronary syndromes indicates recent activation and amplification of the immune response within plaques. This may result in a burst of inflammatory products with tissue degrading and vasoactive properties and, hence, could initiate or accelerate the onset of an acute coronary event.

L13 ANSWER 9 OF 13 MEDLINE on STN
AN 1998090233 MEDLINE
DN PubMed ID: 9430368
TI Systemic inflammatory responses in acute coronary syndrome: increased activity observed in polymorphonuclear leukocytes but not **T lymphocytes.**
AU Takeshita S; Isshiki T; Ochiai M; Ishikawa T; Nishiyama Y; Fusano T; Toyoizumi H; Kondo K; Ono Y; Sato T
CS Department of Medicine, Teikyo University School of Medicine, Tokyo, Japan.. satoshi-t@in.aix.or.jp
SO Atherosclerosis, (1997 Dec) Vol. 135, No. 2, pp. 187-92. Journal code: 0242543. ISSN: 0021-9150.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
ED Entered STN: 17 Feb 1998
Last Updated on STN: 17 Feb 1998
Entered Medline: 5 Feb 1998
AB BACKGROUND: Local inflammation within the coronary arteries is involved in the pathogenesis of acute coronary syndrome. However, the contribution of

a systemic inflammatory response to the pathogenesis of this syndrome has not been well characterized. Accordingly, we investigated systemic inflammatory responses in patients with acute coronary syndrome. METHODS: A total of 83 patients with ischemic heart disease (15 with stable exertional **angina** and 68 with acute coronary syndrome) were studied. The luminol-dependent chemiluminescence (CL) response of polymorphonuclear leukocytes (PMNs), which reflects their ability to generate oxygen species, was used as a marker for PMN activation. Soluble **interleukin**-2 receptor (sIL-2R) levels were measured to assess **T-lymphocyte** activation. RESULTS: CL counts of whole blood from patients with acute coronary syndrome were twice those of patients with stable **angina** (2.38 +/- 0.22 vs 1.10 +/- 0.17 x 10(6) counts, $P < 0.05$). A comparison of CL counts between patients with unstable **angina** and those with acute myocardial infarction revealed no significant differences. **T-lymphocyte** activity, measured by serum sIL-2R, was significantly lower in patients with acute coronary syndrome than those with stable **angina** (214.3 +/- 11.5 vs. 358.3 +/- 115.7 U/ml, $P < 0.05$). CONCLUSIONS: This investigation shows that there is a systemic increase in PMN activity and a decrease in **T-lymphocyte** activity in patients with acute coronary syndrome. This contrasts with the pattern of cellular activation seen at sites of local inflammation within atherosclerotic plaques, suggesting that two independent inflammatory processes (local and systemic) may be involved in the pathogenesis of this syndrome.

L13 ANSWER 10 OF 13 MEDLINE on STN
AN 97261213 MEDLINE
DN PubMed ID: 9107167
TI Acute **T-cell** activation is detectable in unstable **angina.**
AU Neri Serneri G G; Prisco D; Martini F; Gori A M; Brunelli T; Poggesi L; Rostagno C; Gensini G F; Abbate R
CS Clinica Medica Generale e Cardiologia, Florence, Italy.
SO Circulation, (1997 Apr 1) Vol. 95, No. 7, pp. 1806-12.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; AIDS
EM 199705
ED Entered STN: 23 May 1997
Last Updated on STN: 23 May 1997
Entered Medline: 13 May 1997
AB BACKGROUND: Recent studies suggest a role for inflammation in the pathophysiology of unstable **angina.** This study was designed to investigate whether circulating lymphocytes are involved in the inflammatory reaction associated with the episodes of unstable **angina.** METHODS AND RESULTS: Twenty-nine patients with proven unstable **angina**, 36 with stable **angina**, and 30 healthy subjects were studied. Both early and short-lived (**interleukin** -2 receptor [IL-2R], alpha-chain CD25, and transferrin receptor CD71) and late antigen (HLA-DR) expression were investigated by flow cytometric analysis. Soluble IL-2R (sIL-2R) was also measured in plasma by ELISA. Lymphocyte activation was studied at day 1 of hospital admission and after 7, 15, 30, 60, and 90 days. In patients with unstable **angina**, the number of HLA-DR+ CD3 lymphocytes and levels of sIL-2R were higher ($P < .001$) than in patients with stable **angina** and control subjects. Both CD4+ and CD8+ lymphocytes expressed HLA-DR antigens. No differences were found among the different groups of subjects in regard to the expression of CD25 and CD71. Lymphocyte activation was more marked in patients with urgent revascularization. No relationships were found between the number of HLA-DR+ lymphocytes and either the severity of coronary angiographic lesions or the number of ischemic episodes. Observations over time showed a gradual decrease in the number of HLA-DR+ lymphocytes and sIL-2R levels from weeks 3 through 8 to 12. CONCLUSIONS:

The present results indicate that (1) CD4+ and CD8+ circulating lymphocytes are activated in patients with unstable **angina**, and their activation state lasts 6 to 8 weeks; and (2) activation of lymphocytes is not a consequence of myocardial ischemia. These results support the immune system-mediated inflammatory nature of unstable **angina**.

L13 ANSWER 11 OF 13 MEDLINE on STN
AN 97192236 MEDLINE
DN PubMed ID: 9040055
TI Plasma levels of the monocyte chemotactic and activating factor/monocyte chemoattractant protein-1 are elevated in patients with acute myocardial infarction.
AU Matsumori A; Furukawa Y; Hashimoto T; Yoshida A; Ono K; Shioi T; Okada M; Iwasaki A; Nishio R; Matsushima K; Sasayama S
CS Department of Cardiovascular Medicine, Kyoto University, Sakyo-ku, Japan.
SO Journal of molecular and cellular cardiology, (1997 Jan) Vol. 29, No. 1, pp. 419-23.
Journal code: 0262322. ISSN: 0022-2828.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 9 Jun 1997
Last Updated on STN: 9 Jun 1997
Entered Medline: 27 May 1997
AB Cardiac inflammatory responses appear to play a pivotal role in scar formation after acute myocardial infarction. Monocyte chemotactic and activating factor (MCAF) monocyte chemoattractant protein-1 (MCP-1) is a **cytokine** with chemotactic activity for mononuclear phagocytes, but also for NK cells, **T cells**, mast cells, and basophils.
To investigate the possible involvement of MCAF/MCP-1 in the pathogenesis, its course was studied in patients with acute myocardial infarction. Twenty-three consecutive patients with acute myocardial infarction and 18 patients with **angina** pectoris were studied. **Cytokines** were measured by enzyme-linked immunosorbent assay. Plasma levels of **interleukin** IL-1alpha, IL-1beta, and IL-2 were below the detection limit of our method. IL-6 and **interferon**-gamma were detected in 17.4%, and tumor necrosis factor-alpha in 13.0% of patients with acute myocardial infarction, but the frequency was not statistically significantly different from that in **angina** pectoris. The plasma level of MCAF/MCP-1 in myocardial infarction tended to increase at 3 h after the onset of chest pain (133 +/- 19 pg/ml, P= 0.06) and was significantly elevated at 9 h (143 +/- 20 pg/ml) when compared with that in **angina** pectoris (87 +/- 6 pg/ml, P<0.05). The MCAF/MCP-1 level remained increased during the 24-hours observation period (P<0.01), and maximum level (168 +/- 13 pg/ml) was seen at 24 hour. The level of MCAF/ MCP-1 correlated significantly with the plasma level of another chemokine, IL-8, at 12 h after the onset of chest pain (r=0.51, P<0.05), suggesting that common stimuli mediate the release of both **cytokines** in myocardial infarction. The identification of MCAF/MCP-1 as an inflammatory mediator in acute myocardial infarction suggests that mononuclear phagocytes may play an important role in the early stage of the disease.

L13 ANSWER 12 OF 13 MEDLINE on STN
AN 95103715 MEDLINE
DN PubMed ID: 7805203
TI **T lymphocyte** activation in stable **angina** pectoris and after percutaneous transluminal coronary angioplasty.
AU Blum A; Sclarovsky S; Shohat B
CS Coronary Care Unit, Beilinson Medical Center, Petah Tiqva, Israel.

SO Circulation, (1995 Jan 1) Vol. 91, No. 1, pp. 20-2.
Journal code: 0147763. ISSN: 0009-7322.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199502
ED Entered STN: 15 Feb 1995
Last Updated on STN: 15 Feb 1995
Entered Medline: 1 Feb 1995
AB BACKGROUND: Inflammatory reactions have an important part in atherosclerosis. Smooth muscle cells, endothelial cells, monocytes, and **T lymphocytes** are actively involved. The purpose of this study was to assess whether **T lymphocytes** are activated in patients with stable **angina** pectoris who are candidates for a percutaneous transluminal coronary angioplasty (PTCA) and the influence of PTCA on this process. METHODS AND RESULTS: Twenty-four patients participated in the study. All were 40- to 60-year-old men, and all but one underwent successful PTCA. Blood samples were taken 1 day before PTCA and 1 week, 1 month, and 2 months after. Two groups of patients were detected: group A, 11 patients who had high levels of soluble **interleukin**-2 receptor (sIL-2R) before PTCA that decreased toward normal during the follow-up period in most of them; and group B, 13 patients who did not have elevated sIL-2R levels before PTCA and in whom sIL-2R levels did not change after the procedure. Group C consisted of 15 healthy men whose sIL-2R levels were in the normal range (control subjects). CONCLUSIONS: (1) **T lymphocytes** are activated in stable **angina** patients. (2) The level of sIL-2R can be a reliable laboratory marker for follow-up of patients after PTCA, especially those with high sIL-2R levels before the procedure.

L13 ANSWER 13 OF 13 MEDLINE on STN
AN 91368708 MEDLINE
DN PubMed ID: 1892066
TI Coronary atherosclerotic plaques with and without thrombus in ischemic heart syndromes: a morphologic, immunohistochemical, and biochemical study.
AU Arbustini E; Grasso M; Diegoli M; Pucci A; Bramerio M; Ardissino D; Angoli L; de Servi S; Bramucci E; Mussini A; +
CS Department of Pathology, Universita di Pavia, Italy.
SO The American journal of cardiology, (1991 Sep 3) Vol. 68, No. 7, pp. 36B-50B.
Journal code: 0207277. ISSN: 0002-9149.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199110
ED Entered STN: 3 Nov 1991
Last Updated on STN: 3 Nov 1991
Entered Medline: 11 Oct 1991
AB We investigated incidence, severity, and distribution of coronary atherosclerosis, acute thrombosis, and plaque fissuring in ischemic heart disease (both unstable-acute syndromes and chronic ischemia) and in nonischemic controls. We also studied the structural, immunohistochemical, and biochemical profile of plaques, with and without thrombus, including morphometry, immunophenotyping of inflammatory infiltrates, **cytokine** presence, and ultrastructural features. Critical coronary stenosis was almost the rule in both acute and chronic ischemic series (greater than 90%) whereas it reached 50% in control subjects. Thrombosis was principally characteristic of unstable-acute ischemic syndromes (unstable **angina**, 32%; acute myocardial infarction, 52%; cardiac sudden death, 26%) but was also found in chronic ischemia (stable **angina**, 12%; ischemic cardiomyopathy, 14%) and in control subjects (4%). Plaque fissuring without thrombus occurred in

low percentages in lipid-rich, severe eccentric plaques in most series. Major differences were found between pultaceous-rich versus fibrous plaques rather than between plaques with or without thrombus. Pultaceous-rich plaques were frequent in sites of critical stenosis, thrombosis, and ulceration. Inflammatory infiltrates, i.e., **T cells**, macrophages, and a few beta cells, mostly occurred in lipid-rich, plaques unrelated to thrombus. In adventitia, infiltrates were a common finding unrelated to any syndrome. Necrotizing **cytokines** such as alpha-TNF were immunohistochemically detected in macrophages, smooth muscle, and intimal cells and detected by immunoblotting in 67% of pultaceous-rich plaques, either with or without thrombus. Immune response mediators such as IL-2 were also expressed in analogous plaques but in a minor percentage (50%-40%). Media were extensively damaged in severely diseased vessels with and without thrombus. Ultrastructural study showed that the fibrous cap was either highly cellular or densely fibrillar. Intimal injury with collagen exposure was often associated with platelet adhesion, whereas foamy cell exposure was not. In conclusion, investigated parameters were essentially similar in plaques, both with and without thrombus, whereas major differences were found between pultaceous-rich and fibrous plaques. Since platelets adhere to exposed collagen and not to foam cells, the type of exposed substrates could play a major role in thrombosis.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.54	7.75

STN INTERNATIONAL LOGOFF AT 12:14:24 ON 24 APR 2006